

# Recommendation to Waive Pre-Approval Inspection Memo - Seraclone Blood Grouping Reagent Anti-S (Monoclonal)

Date: July 29, 2008  
 From: Marion Michaelis, Reviewer, OCBQ/DMPQ/MRB II, HFM-676  
 To: Administrative Bundled File, Biotest AG (LIC #1702):

Products for use on the Tango Automated Blood Group Analyzer

| (STN)           | Biological Products   | Cell Line(s)    | Strip Proprietary Name      |
|-----------------|---|-----------------|-----------------------------|
| BL<br>125097/10 | Blood Grouping Reagent, Anti-D (Monoclonal)(IgM) (Formulated for Automated Testing) | BS226           | Component of Erytype S Rh+K |
|                 | Blood Grouping Reagent, Anti-D (Monoclonal)(IgM) (Formulated for Automated Testing) | BS232           | Component of Erytype S Rh+K |
| BL<br>125206/0  | Blood Grouping Reagent, Anti-C (Monoclonal) (Formulated for Automated Testing)      | MS24/P3x25513G8 | Component of Erytype S Rh+K |
| BL<br>125202/0  | Blood Grouping Reagent, Anti-E (Monoclonal) (Formulated for Automated Testing)      | MS260/MS12      | Component of Erytype S Rh+K |
| BL<br>125205/0  | Blood Grouping Reagent, Anti-c (Monoclonal)   | MS33            | Component of Erytype S Rh+K |

| <b>(STN)</b> | <b>Biological Products</b>   | <b>Cell Line(s)</b> | <b>Strip Proprietary Name</b> |
|--------------|--|---------------------|-------------------------------|
|              | (Formulated for Automated Testing)   |                     |                               |
| BL 125203/0  | Blood Grouping Reagent, Anti-e (Monoclonal) (Formulated for Automated Testing) | MS16/MS21/ MS63     | Component of Erytype S Rh+K   |
| BL 125204/0  | Blood Grouping Reagent, Anti-K (Monoclonal) (Formulated for Automated Testing) | MS56                | Component of Erytype S Rh+K   |

NOTE- Erytype S are strip wells (eight wells per strip) containing: Anti-D, Anti-D, Anti-C, Anti-c, Anti-E, Anti-e and Anti-K+ Neg Cont

| <b>BL 125208/0</b>                             | <b>Reagent Red Blood Cells For Use in Automated Systems</b> | <b>Cell Line(s)</b> |
|--|---|---------------------|
|  | Erytypecell A 1 and B                                       | N/A                 |
|  | Biotestcell Pool;<br>Biotestcell 1, 2;<br>Biotestcell 3     | N/A                 |
|  | Biotestcell I8;<br>Biotestcell I11                          | N/A                 |
| BL 125218/0                                    | Blood Grouping Reagent Anti-D (Monoclonal) (IgG Blend)      | BS221/H4111B7       |
| Seraclone- Liquid BGR for manual tube testing: |   |                     |
| BL 125217/0                                    | Blood Grouping Reagent, Anti-Jk b                           | MS8                 |

| <b>BL<br/>125208/0</b> | <b>Reagent Red Blood<br/>Cells For Use in<br/>Automated Systems</b> | <b>Cell Line(s)</b> |
|------------------------|---|---------------------|
|                        | (Monoclonal)  |                     |
| BL<br>125231/0         | Blood Grouping<br>Reagent, Anti-Jk a<br>(Monoclonal)                | MS15                |
| BL<br>125219/0         | Blood Grouping<br>Reagent, Anti-A<br>(Murine Monoclonal)            | A003                |
| BL<br>125220/0         | Blood Grouping<br>Reagent, Anti-B<br>(Murine Monoclonal)            | B005                |
| BL<br>125221/0         | Blood Grouping<br>Reagent, Anti-A,B<br>(Murine Monoclonal)          | BS63 and BS85       |
| BL<br>125224/0         | Blood Grouping<br>Reagent, Anti-M<br>(Murine Monoclonal)            | BS57                |
| BL<br>125225/0         | Blood Grouping<br>Reagent, Anti-N<br>(Murine Monoclonal)            | BS41                |
| BL<br>125230/0         | Blood Grouping<br>Reagent, Anti-K<br>(Monoclonal)                   | MS56                |
| BL<br>125232/0         | Blood Grouping<br>Reagent, Anti-k<br>(Murine Monoclonal)            | Lk1                 |
| BL<br>125233/0         | Blood Grouping<br>Reagent, Anti-Le a<br>(Murine Monoclonal)         | LEA2                |
| BL<br>125213/0         | Blood Grouping<br>Reagent, Anti- P 1<br>(Murine Monoclonal)         | 650                 |

Other Reagents for Manual Tubes Testing

| <b>(STN)</b>      | <b>Anti-Human Globulin</b>                                   | <b>Cell Line(s)</b> |
|-------------------|--|---------------------|
| BL<br>125242/0    | Anti-Human Globulin<br>(Rabbit/Murine<br>Monoclonal)         | BRIC-8              |
| BL<br>125215/0    | Anti-Human Globulin  | N/A                 |
| <b>BL125098/8</b> | Anti-Human Globulin<br>(Formulated for Automated<br>Testing) | <b>N/A</b>          |
| <b>(STN)</b>      | <b>Reagent Red Blood Cells</b>                               | <b>Cell Line(s)</b> |
| BL<br>125207/0    | Biotestcell A 1 and B  | N/A                 |
|                   | Biotestcell A 2  | N/A                 |
|                   | Biotestcell Pool; Biotestcell<br>1, 2; Biotestcell 3         | N/A                 |
|                   | Biotestcell I8; Biotestcell<br>I11                           | N/A                 |

Applicant: Biotest AG, Dreieich, Germany location.

Products: See above bundled file listing.

Through: Chiang Syin, Ph.D., Branch Chief, OCBQ/DMPQ/MRB II, HFM-676

### Concurrent Clearance Routing

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 John A. Eltermann, Jr., R.Ph., M.S.  
 Director, Division of Manufacturing and Product  
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 Date CONCUR

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 DO NOT  
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Acting Director, Division of Hematology, HFM-370  
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DO NOT  
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## Summary

We recommend waiver of the pre-approval inspection, BLAs and BLS for Biotest AG, for manufacturing multiple new Blood Grouping Reagents, Anti-Human Globulin, and Reagent Red Blood Cells (specified above).

## Brief History

Biotest AG, U.S. License 1702, Dreieich, Germany, submitted a bundle consisting of 30 new BLAs and 2 BLSs in September 2006 (see above). Biotest is currently licensed to manufacture several Erytype S Blood Grouping Reagents are for use on the TANGO Automated Blood Bank System. The purpose of this submission is to obtain approval for additional monoclonal antibodies as components of Erytype S plates, to update the CMC with information related to sublotting and testing of bulk antibodies, and to obtain approval for a complete line of liquid reagents for use in manual immunohematology tube tests.

This bundle is a companion submission to 4 BLAs for Blood Grouping Reagents (Monoclonal)(For Further Manufacturing Use)(FFMU) submitted by DIAGAST, U.S. License 1744; and 10 BLSs and 2 BLAs for Blood Grouping Reagents (Monoclonal)(For Further Manufacturing Use)(FFMU)and Anti-Human Globulin (Murine Monoclonal)(For Further Manufacturing Use)(FFMU) submitted by Millipore (Celliance) U.S. License 1721. The BLAs/BLSs were submitted by DIAGAST and Millipore in September 2006.

## Description of Change:

- BLAs for manufacturing new Blood Grouping Reagents, Anti-Human Globulin, and Reagent Red Blood Cells (specified above) and associated process and manufacturing changes to previously licensed BGR's.

## Basis for the Waiver:

This waiver is based on criteria outlined in Center wide SOPP 8410 "Determining When Pre-Licensing/Pre-Approval Inspections are Necessary." As stated in that SOPP, it is CBER's policy that a pre-license or pre-approval inspection will generally be necessary for an application if any of the following criteria in bold are met:

- The facility does not hold an active US license.

Biotest AG, Dreieich, Germany does hold U.S. license No. 1702.

- The FDA has not inspected the facility in the last two years.

This facility (Dreieich, Germany) in the last two years was inspected by:

1. The first inspection was conducted by Team Biologics (Jacqueline Diaz Albertini) during the time period of 19-28 September 2006 and was a GMP inspection done as part of the Team Biologics work-plan for FY 2006.
  2. The second inspection was conducted by CBER (Susan Yu and Joanne Pryzbylik) during the week of June 28 through July 6, 2004 and was a Pre-Licensing Inspection (PLI) for the manufacture of Blood Grouping Reagents (BGR) and Anti-Human Globulin (AHG) for use on the TANGO, an automated blood bank analyzer.
- **The previous inspection(s) revealed significant GMP violations in areas related to the processes in the submission (similar processes) or systemic problems, such as QC/QA oversight.**
    1. The inspection in September 2006 was classified VAI. The GMP inspection was done as part of the Team Biologics work-plan for FY 2006.
    2. The inspection in June-July 2004 was classified VAI. The PLI inspection was conducted for the manufacture of Blood Grouping Reagents (BGR) and Anti-Human Globulin (AHG) for use on the TANGO, an automated blood bank analyzer.
  - **The establishment is performing significant manufacturing step(s) in new (unlicensed) areas using different equipment (representing a process change). This would include areas that are currently dedicated areas that have not been approved as multi-product facilities/buildings/areas.**

All areas used for the manufacturing are licensed areas.

- **The manufacturing process is sufficiently different (new production methods), specialized equipment or facilities) from that of other approved products produced by the establishment.**

The production process is similar to other immunohematology reagents and systems for blood grouping, phenotyping, and antibody screening products produced at the facility.

#### **Waiver Recommendation:**

Based on the information provided in the BLA and related correspondence supporting the overall compliance status of the license holder, the review committee recommends waiving the pre-approval inspection for the facility changes associated with these supplements.

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07/29/08

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Marion Michaelis, HFM-676  
Reviewer, DMPQ